

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Dennis A. Carson et al.

Title: USE OF ETODOLAC TO TREAT HYPERPLASIA

Docket No.: 103.032US1

Filed: September 19, 2003

Examiner: Unknown

Customer No.: 21186

Serial No.: 10/667,208

Due Date: N/A

Group Art Unit: 1614

Confirmation No.: 7161



Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

We are transmitting herewith the following attached items (as indicated with an "X"):

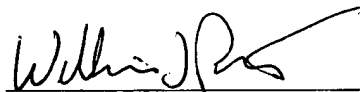
☒ A return postcard.

☒ An Information Disclosure Statement (2 pgs.), Form 1449 (4 pgs.), and copies of 46 cited documents.

If not provided for in a separate paper filed herewith, Please consider this a PETITION FOR EXTENSION OF TIME for sufficient number of months to enter these papers and please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.

Customer Number 21186

By:   
Atty: William F. Prout  
Reg. No. 33,995

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 20th day of January, 2004.

Gulim Abilova  
Name

Gulim Abilova  
Signature

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.  
(GENERAL)

Customer Number 21186

S/N 10/667,208



PATENT

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant:	Dennis A. Carson et al.	Examiner:	Unknown
Serial No.:	10/667,208	Group Art Unit:	1614
Filed:	September 19, 2003	Docket:	103.032US1
Title:	USE OF ETODOLAC TO TREAT HYPERPLASIA		

---

**INFORMATION DISCLOSURE STATEMENT**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

In compliance with the duty imposed by 37 C.F.R. § 1.56, and in accordance with 37 C.F.R. §§ 1.97 *et. seq.*, the enclosed materials are brought to the attention of the Examiner for consideration in connection with the above-identified patent application. Applicants respectfully request that this Information Disclosure Statement be entered and the documents listed on the attached Form 1449 be considered by the Examiner and made of record. Pursuant to the provisions of MPEP 609, Applicants request that a copy of the 1449 form, initialed as being considered by the Examiner, be returned to the Applicants with the next official communication.

Applicants note that U.S. Patent 3,843,681 and DE-2226340 are from the same patent family. A copy of an English abstract of the German patent is included as well.

Pursuant to 37 C.F.R. §1.97(b), it is believed that no fee or statement is required with the Information Disclosure Statement. However, if an Office Action on the merits has been mailed, the Commissioner is hereby authorized to charge the required fees to Deposit Account No. 19-0743 in order to have this Information Disclosure Statement considered.

INFORMATION DISCLOSURE STATEMENT

Serial No :10/667208

Filing Date: September 19, 2003

Title: USE OF ETODOLAC TO TREAT HYPERPLASIA

Page 2

Dkt: 103.032US1

The Examiner is invited to contact the Applicants' Representative at the below-listed telephone number if there are any questions regarding this communication.

The present application is either a U.S. national patent application filed after June 30, 2003 or an international application that entered the national stage under 35 U.S.C. § 371 after June 30, 2003. Thus, Applicant believes that the U.S. Patent & Trademark Office has waived the requirement under 37 C.F.R. 1.98 (a)(2)(i) for submitting a copy of each cited U.S. patent and each U.S. patent application publication. The waiver is provided in a pre-OG notice from the U.S. Patent & Trademark Office entitled "Information Disclosure Statements May Be Filed Without Copies of U.S. Patents and Published Applications in Patent Applications filed after June 30, 2003" and dated July 11, 2003. Applicant acknowledges the requirement to submit copies of foreign patent documents and non-patent literature in accordance with 37 C.F.R. 1.98(a)(2).

Respectfully submitted,

DENNIS A. CARSON ET AL.

By their Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.  
P.O. Box 2938  
Minneapolis, MN 55402  
(612) 373-6968

Date

January 20, 2004

By

William F. Prout

William F. Prout

Reg. No. 33,995

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 20th day of January, 2004.

Name

Gulim Abilova

Signature

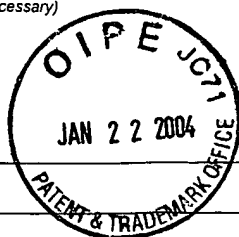
Gulim Abilova

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)



Complete if Known

Application Number 10/667,208

Filing Date September 19, 2003

First Named Inventor Carson, Dennis

Group Art Unit 1614

Examiner Name Unknown

Sheet 1 of 4

Attorney Docket No: 103.032US1

**US PATENT DOCUMENTS**

Examiner Initial *	USP Document Number	Publication Date	Name of Patentee or Applicant of cited Document	Class	Subclass	Filing Date If Appropriate
	US-3,843,681	10/22/1974	Demerson, C. A., et al.	260	326.14 R	06/01/1971
	US-4,337,760	07/06/1982	Rubin, D.	128	1 R	10/31/1979
	US-5,561,151	10/01/1996	Young, J. W., et al.	514	411	01/04/1995
	US-5,811,558	09/22/1998	Adger, B. M., et al.	548	427	04/11/1995
	US-5,939,455	08/17/1999	Rephaeli, Ada	514	547	03/11/1997
	US-5,955,504	09/21/1999	Wechter, William J., et al.	514	568	03/13/1995
	US-6,066,741	05/23/2000	Vigano, E., et al.	548	432	09/08/1998
	US-6,545,034	04/01/2003	Carson, et al.	514	411	07/23/1999

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Foreign Document No	Publication Date	Name of Patentee or Applicant of cited Document	Class	Subclass	T <sup>2</sup>
	DE-2226340	03/15/1973	Demerson, Christopher A., et al.	C07D	27/56	Abstract only
	EP-0289262	11/02/1986	Venuti, M. C., et al.	C07C	93/00	
	WO-00/02555	01/20/2000	Nardella, Francis A., et al.	A61K	31/40	
	WO-00/13410	03/09/2000	Monroe, D. A.	H04N	5/76	
	WO-96/28148	09/19/1996	Wechter, William J., et al.	A61K	31/19	
	WO-98/09603	03/12/1998	Wechter, William J., et al.	A61K		
	WO-98/18490	05/07/1998	Clynes, M. M.	A61K	45/06	

**OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
		ABRAMSON, S. B., et al., "The Mechanisms of Action of Nonsteroidal Antiinflammatory Drugs", <u>Arthritis &amp; Rheumatism</u> , 32 (1), (Jan. 1989), 1-9	
		ALEXANIAN, R., et al., "The Treatment of Multiple Myeloma", <u>The New England Journal of Medicine</u> , 330 (7), (Feb. 17, 1994), 484-489	
		BARLOGIE, B., et al., "Prognostic Factors with High-Dose Melphalan for Refractory Multiple Myeloma.", <u>Blood</u> , 72, (1988), 2015-2019	
		BATAILLE, R., et al., "Multiple Myeloma", <u>New England Journal of Medicine</u> , 336, (1997), 1657-1664	
		BECKER-SCHARFENKAMP, U., et al., "Evaluation of the Stereoselective Metabolism of the Chiral Analgesic Drug Etodolac by High-Performance Liquid Chromatography", <u>Journal of Chromatography</u> , 621 (2), (Nov. 24, 1993), 199-207	
		BELLOSILLO, B., et al., "Aspirin and Salicylate Induce Apoptosis and Activation of Caspases in B-Cell Chronic Lymphocytic Leukemia Cells", <u>Blood</u> , 92 (4),	

**EXAMINER****DATE CONSIDERED**

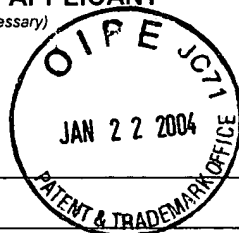
Substitute Disclosure Statement Form (PTO-1449)

\* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 809. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional) 2 Applicant is to place a check mark here if English language Translation is attached

Substitute for form 1449A/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)



Complete if Known

**Application Number** 10/667,208

**Filing Date** September 19, 2003

**First Named Inventor** Carson, Dennis

**Group Art Unit** 1614

**Examiner Name** Unknown

Sheet 2 of 4

**Attorney Docket No:** 103.032US1

**OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
		(Aug. 15, 1998), 1406-1414	
		BERENDES, U., et al., "Simultaneous Determination of the Phase II Metabolites of the Non Steroidal Anti-inflammatory Drug Etodolac in Human Urine", <u>Enantiomer</u> , 1, Abstract Only, Chemical Abstracts, Abstract No. 126:207064q, (1996), 415-422	
		BRENNAN, E., et al., "New Enzymatic and Chemical Approaches to Enantiopure Etodolac", <u>Tetrahedron</u> , 53, (1997), 17769-17780	
		BROCKS, D. R., et al., "Etodolac Clinical Pharmacokinetics", <u>Clinical Pharmacokinetics</u> , 26 (4), (1994), 259-274	
		CARSON, D. A., et al., "Oral Antilymphocyte Activity and Induction of Apoptosis by 2-chloro-2'-arabino-fluoro-2'-deoxyadenosine", <u>Proc. Natl. Acad. Sci. USA</u> , 89 (7), (Apr. 1992), 2970-2974	
		CHINETTI, G., et al., "Activation of Proliferator-activated Receptors alpha and gamma Induces Apoptosis of Human Monocyte-derived Macrophages", <u>The Journal of Biological Chemistry</u> , 273 (40), (Oct. 2, 1998), 25573-25580	
		CUNNINGHAM, D., et al., "High-dose Melphalan for Multiple Myeloma: Long-term Follow-up Data", <u>Journal of Clinical Oncology</u> , 12, (1994), 764-768	
		DEMERSON, C. A., et al., "Etodolic Acid and Related Compounds. Chemistry and Antiinflammatory Actions of Some Potent Di- and Trisubstituted 1,3,4,9-Tetrahydropyrano[3,4-b]indole-1-acetic Acids", <u>Journal of Medicinal Chemistry</u> , 19 (3), (1976), 391-395	
		DEMERSON, C. A., et al., "Resolution of Etodolac and Antiinflammatory and Prostaglandin Synthetase Inhibiting Properties of the Enantiomers", <u>J. Med. Chem.</u> , 26 (12), (Dec. 1983), 1778-1780	
		DRACHENBERG, D. F., et al., "Treatment of Prostate Cancer: Watchful Waiting, Radical Prostatectomy, and Cryoablation", <u>Seminars in Surgical Oncology</u> , 18 (1), (Jan/Feb. 2000), 37-44	
		DUFFY, C. P., et al., "Enhancement of Chemotherapeutic Drug Toxicity to Human Tumour Cells In Vitro by a Subset of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)", <u>European Journal of Cancer</u> , 34 (8), (July 1998), 1250-1259	
		HAHNFELD, L. E., et al., "Prostate Cancer", <u>The Medical Clinics of North America - The Aging Male Patient</u> , 83 (5), (Sept. 1999), 1231-1245	
		HAROUSSEAU, J. L., et al., "Double-Intensive Therapy in High-Risk Multiple Myeloma", <u>Blood</u> , 79 (11), (June 1, 1992), 2827-2833	
		KRAJEWSKI, S., et al., "Detection of Multiple Antigens on Western Blots", <u>Analytical Biochemistry</u> , 236 (2), Article No. 0160, (May 1996), 221-228	
		LANDIS, S. H., et al., "Cancer Statistics, 1998", <u>CA Cancer J. Clin.</u> , 48 (1), (1998), 6-29	
		LEE, D. H., "Proteasome Inhibitors: Valuable New Tools For Cell Biologists", <u>Trends in Cell Biology</u> , 8, (October 1998), 397-403	
		LEHMANN, J. M., et al., "Peroxisome Proliferator-activated Receptors alpha and	

**EXAMINER**

**DATE CONSIDERED**

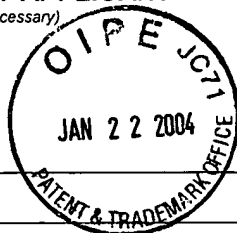
Substitute Disclosure Statement Form (PTO-1449)

\* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional) 2 Applicant is to place a check mark here if English language Translation is attached

Substitute for form 1449A/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)



Sheet 3 of 4

Complete if Known

Application Number 10/667,208

Filing Date September 19, 2003

First Named Inventor Carson, Dennis

Group Art Unit 1614

Examiner Name Unknown

Attorney Docket No: 103.032US1

**OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
		Y Are Activated by Indomethacin and Other Non-steroidal Anti-inflammatory Drugs", <u>The Journal of Biological Chemistry</u> , 272 (6), (Feb. 7, 1997), 3406-3410	
		LEMAN, EDDY S., et al., "Characterization of the Nuclear Matrix Proteins in a Transgenic Mouse Model for Prostate Cancer", <u>Journal of Cellular Biochemistry</u> , 86, (2002), 203-212	
		LEONI, L. M., et al., "Induction of an Apoptotic Program in Cell-Free Extracts by 2-Chloro-2'-deoxyadenosine 5'-triphosphate and Cytochrome C", <u>PNAS, USA</u> , 95 (16), (Aug. 4, 1998), 9567-9571	
		LOCHMULLER, C. H., et al., "Chromatographic Resolution of Enantiomers -- Selective Review", <u>Journal of Chromatography</u> , 113 (3), (Oct. 22, 1975), 283-302	
		MARTEL, R. R., et al., "Anti-inflammatory and Analgesic Properties of Etodolic Acid in Rats", <u>Canadian Journal of Physiology and Pharmacology</u> , 54 (3), (June 1976), 245-248	
		MOONEY, P. T., et al., "Cell Pathways' Exisulind 'Aptosyn' Demonstrates Potential to Delay Hormone Therapy in Post-Prostatectomy Men at Risk of Prostate Cancer Recurrence", <a href="http://biz.yahoo.com/bw/000501/ga_cell_pa_1.html">http://biz.yahoo.com/bw/000501/ga_cell_pa_1.html</a> , (May 2000), 3 pages	
		NARDELLA, FRANCIS A., et al., "Enhanced Clearance of Leukemic Lymphocytes in B Cell Chronic Lymphocytic Leukemia (CLL) with Etodolac", <u>Arthritis &amp; Rheumatism</u> , 42 (9) Supplement, Abstract No. 41, (Sept. 1999), page S56	
		RICOTE, M., et al., "The Peroxisome Proliferator-Activated Receptor-Y is a Negative Regulator of Macrophage Activation", <u>Nature</u> , 391, (Jan. 1, 1998), 79-82	
		RIEDEL, D. A., et al., "The Epidemiology of Multiple Myeloma", <u>Hematology/Oncology Clinics of North America</u> , Multiple Myeloma, 6 (2), (April 1992), 225-247	
		ROYALL, J. A., et al., "Evaluation of 2',7'-Dichlorofluorescein and Dihydrorhodamine 123 as Fluorescent Probes for Intracellular H2O2 in Cultured Endothelial Cells", <u>Archives of Biochemistry and Biophysics</u> , 302 (2), (May 1, 1993), 348-355	
		SHIFF, S. J., et al., "Nonsteroidal Antiinflammatory Drugs Inhibit the Proliferation of Colon Adenocarcinoma Cells: Effects on Cell Cycle and Apoptosis", <u>Experimental Cell Research</u> , 222, Article No. 0023,(1996), 179-188	
		TANG, D. G., et al., "Target to Apoptosis: A Hopeful Weapon for Prostate Cancer", <u>The Prostate</u> , (1997), 284-293	
		VAN BREEMEN, R. B., et al., "Characterization of Oxygen-Linked Glucuronides by Laser Desorption Mass Spectrometry", <u>Biomed. Mass Spectrom.</u> , 11, Abstract Only, Chemical Abstracts, Abstract No. 101:106777c,(1984), 278-283	
		VENUTI, M. C., et al., "Synthesis and Biological Evaluation of omega-(N,N,N-trialkylammonium)alkyl Esters and Thioesters of Carboxylic Acid Nonsteroidal	

**EXAMINER****DATE CONSIDERED**

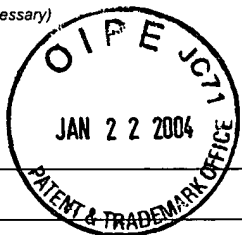
Substitute Disclosure Statement Form (PTO-1449)

\* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional) 2 Applicant is to place a check mark here if English language Translation is attached

Substitute for form 1449A/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)



Complete if Known

Application Number 10/667,208

Filing Date September 19, 2003

First Named Inventor Carson, Dennis

Group Art Unit 1614

Examiner Name Unknown

Sheet 4 of 4

Attorney Docket No: 103.032US1

**OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
		Antiinflammatory Agents", <u>Pharm. Res.</u> , <u>6</u> , Abstract Only, Chemical Abstracts, Abstract No. 112:111681y, (1989), 867-873	
		WANG, X., et al., "Antipoptotic Action of 1,25-Dihydroxyvitamin D3 Is Associated with Increased Mitochondrial MCL-1 and RAF-1 Proteins and Reduced Release of Cytochrome c", <u>Experimental Cell Research</u> , <u>235</u> (1), Article No. EX973667, (1997), 210-217	
		WECHTER, W. J., et al., "E-7869 (R-Flurbiprofen) Inhibits Progression of Prostate Cancer in the TRAMP Mouse", <u>Cancer Research</u> , <u>60</u> , (April 15, 2000), 2203-2208	
		WEISS, H. A., et al., "Aspirin, Non-Steroidal Anti-Inflammatory Drugs and Protection from Colorectal Cancer: a Review of the Epidemiological Evidence", <u>Scandinavian Journal of Gastroenterology</u> , <u>31</u> (Suppl. 220), (1996), 137-141	
		WILEN, S. H., et al., "Strategies In Optical Resolutions", <u>Tetrahedron</u> , <u>33</u> (21), Tetrahedron Report Number 38, (1977), 2725-2736	

**EXAMINER****DATE CONSIDERED**

Substitute Disclosure Statement Form (PTO-1449)

\* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional) 2 Applicant is to place a check mark here if English language Translation is attached